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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,332	06/21/2002	Kenneth J. Ruthschild	AMBER-06797	3619

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EXAMINER

KATCHEVES, KONSTANTINA T

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/049,332

Applicant(s)

RUTHSCHILD ET AL.

Examiner

Konstantina Katcheves

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2005.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-68 is/are pending in the application.
4a) Of the above claim(s) 1-20 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 21-68 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 21 June 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-68 are pending in the instant application. Claims 1-20 have been withdrawn from consideration. Claims 21-68 are currently under examination.

Election/Restrictions

Applicant's election without traverse of Group IV, claims 21-68, in the reply filed on 10 February 2005 is acknowledged. Claims 1-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10 February 2005.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-16 of copending Application No. 10/174368 (Application '368). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of Application '368 are drawn to a species of the instant claims such that the inventions of the instant claims are anticipated by Application '368.

The invention of the instant claims is generally drawn to a gel free method a) providing i) a misaminoacylated initiator tRNA molecule, said misaminoacylated initiator tRNA molecule comprising a first marker, and ii) a nucleic acid template encoding a protein, said protein comprising an affinity marker and a C-terminal marker, and b) introducing said misaminoacylated initiator tRNA to a translation system comprising said template under conditions such that a nascent protein is generated, said protein comprising said first marker, said affinity marker, and said C-terminal markers, and c) testing said nascent protein under gel-free conditions.

The invention of Application '368 is drawn to a gel-free method comprising: a) providing i) a sample comprising template nucleic acid, ii) primers capable of introducing sequences encoding an N-terminal marker and a C-terminal marker into said template nucleic acid so as to create modified template, and iii) a misaminoacylated tRNA comprising a biotin marker, and iv)

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a translation system; b) diluting at least a portion of said sample to create a plurality of diluted samples at least a portion of which contains some template; c) amplifying said plurality of diluted samples with said primers under conditions such that said sequences encoding said N-terminal and C-terminal markers are introduced into at least some of said nucleic acid template such that modified template encoding a protein is produced as an amplification product; d) introducing said modified template into said translation system under conditions such that a nascent protein is generated, said protein comprising at least said N-terminal marker; and e) isolating said nascent protein from said translation system by binding said nascent protein to a biotin-binding ligand, and f) testing said nascent protein under gel-free conditions that permit the detection of a truncated protein.

Application '368 discloses a the method steps of the present application wherein provided to a translation system (step c) are a misaminoacylated tRNA with a biotin marker (step a(iii)), a nucleic acid encoding a protein with a N terminal and C terminal marker (step a(iv)) and testing said protein under gel-free conditions that permit identification of a truncated protein (step (d)). Thus, the claims of Application '368 anticipate the claims of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 21-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33-43 of copending Application No. 10/339712 (Application '712) in view of Rothschild et al. (WO 01/14578 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other

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because the invention of the instant claims would have been obvious over the invention described in the claims of Application '712.

The invention of the instant claims is drawn to a method as described above.

Application '712 discloses a method comprising (a) providing (i) an amplified template coding for a protein having a c-terminal and N-terminal marker, (ii) an misaminoacylated tRNA comprising an affinity marker (iii) a translation system; and (b) introducing the template and misaminoacylated tRNA into said translation system. The method of Application '712 fails to disclose that the protein is measured in a gel-free system.

Rothschild et al teaches a gel-free method of detecting a truncated protein that involves amplification of a nucleic acid template with primers harboring N- and C- terminal markers, introduction of the amplified DNA in translation reaction and detecting the nascent protein (page 1 18, lines 1-29 bridging page 1 19, lines 1-9). In addition they teach different types of nascent proteins such as recombinant gene products and enzymes (page 8, lines 6-10), a cellular or cell-free translation system, various type of cellular translation systems such as tissue culture cells and primary cells, various types of cell-free translation systems such as wheat germ extracts and insect cell lysates and a cell-free system that is a continuous flow or dialysis system with an incubation temperature between about 25C to 45C (page 10 lines 19-20, page 24, lines 28-29, page 25, lines 12-20, page 28 lines 12-26, page 148, lines 19-21). Rothschild et al teaches a gel-free method of detecting a truncated protein that involves amplification of a nucleic acid template with primers harboring N- and C-terminal markers, introduction of the PCR amplified DNA and a biotin-lysyl-tRNxYs which reads on a misaminoacylated tRNA with a biotin marker into a translation system, isolation of nascent protein using streptavidin which is a biotin-binding

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ligand and detection of the nascent protein for truncations using measured ratios of the N- and C-terminal markers in a gel-free method (page 50, lines 26-30 bridging page 51, lines 1-5, page 125-129, Example 25).

The invention of the instant claims would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the claims of Application '712. One of ordinary skill in the art would have been motivated to use a gel-free system of detection given the disclosure of Rothchild et al. specifically teaching detecting a protein under a gel-free system using the same method steps of Application '712. Therefore, the invention as a whole is an obvious variation of the claims of Application '712.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an

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international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 21-68 are rejected under 35 U.S.C. 102(e) as being anticipated by either US Patent 6,303,337 ('337 Patent) or US Patent 6,306,628 ('628 Patent)

The applied references have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The invention of the instant claims is drawn to a gel-free method of identifying a truncated protein comprising a) providing i) a misaminoacylated initiator tRNA molecule, said misaminoacylated initiator tRNA molecule comprising a first marker, and ii) a nucleic acid template encoding a protein, said protein comprising an affinity marker and a C-terminal marker, and b) introducing said misaminoacylated initiator tRNA to a translation system comprising said template under conditions such that a nascent protein is generated, said protein comprising said first marker, said affinity marker, and said C-terminal markers, and c) testing said nascent protein under gel-free conditions (Claims 21, 33, 45, and 57). The limitation of claims 23, 35, 47 and 59 comprise cell free or cellular translations systems wherein said systems are from various cell-types (claims 24, 25, 36, 37, 48, 49, 60 and 61). The cell-free system is a continuous flow or dialysis system (claims 27, 39, 51 and 63). The t-RNA is misaminoacylated by chemical or

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enzymatic means (claims 28, 40, 52 and 64). The first marker is a fluorescent marker which is either dipyrrometheneboron difluoride or derivatized coumarin (claims 30, 31, 42, 43, 54, 55, 66 and 67). The C-terminal comprises a his-tag (claims 32, 44, 56, and 68).

Rothschild et al teaches a gel-free method of detecting a truncated protein that involves amplification of a nucleic acid template with primers harboring N- and C- terminal markers, introduction of the amplified DNA in translation reaction and detecting the nascent protein (See '337 Patent abstract, column 18 and '628 Patent abstract and '628 Patent column 18). In addition they teach different types of nascent proteins such as recombinant gene products and enzymes (See '337 Patent columns 7-8 and '628 Patent columns 7-8), a cellular or cell-free translation system, various type of cellular translation systems such as tissue culture cells and primary cells, various types of cell-free translation systems such as wheat germ extracts and insect cell lysates and a cell-free system that is a continuous flow or dialysis system with an incubation temperature between about 25C to 45C (See '337 Patent column 17 and '628 Patent column 17).

Rothschild et al teaches a gel-free method of detecting a truncated protein that involves amplification of a nucleic acid template with primers harboring N- and C-terminal markers, introduction of the PCR amplified DNA and a biotin-misaminoacylated tRNA which reads on a misaminoacylated tRNA with a biotin marker into a translation system, isolation of nascent protein using streptavidin which is a biotin-binding ligand and detection of the nascent protein for truncations using measured ratios of the N- and C-terminal markers in a gel-free method as well as derivitized coumarin fluorescent markers and his-tag (See '337 Patent column 8, line 19-21 and column 20-21 and See '628 Patent column 8, lines 19-21 and columns 20-21).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31, 43, 55, and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims appear to recite a Markush group without the proper use of the Markush format. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. The metes and bounds of this Markush group are indefinite because it is unclear if the members of this group are mutually exclusive. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925).

Conclusion


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Examiner
Art Unit 1636



JAMES KETTER
PRIMARY EXAMINER